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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,704	07/18/2001	Mark H. Vickers	3911-7	2234

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	

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/ 3

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,704	VICKERS ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 20-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 20-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is in response to the amendment and remarks filed on 6/13/03 in Paper No: 14. Claims 1-12 and 20-28 are pending. Applicant has added claims 20-28 (These are claims 13-21 which have been renumbered under Rule 1.126). Claims 1, 2, 6-8 and 10-12 have been amended.

2. Applicant has amended the title and provided an abstract.

3. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action, has been overcome by Applicant's response and withdrawn.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claim 1-12 and 20-28 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if

experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification describes experiments conducted on a single strain of rat pups (Wistar rats) to study methods to treat hypertension in mammals. At pages 8-10 of the specification it is disclosed that dams were restricted to 30% of *ad-libitum* food intake. However, following the birth of offspring from restricted fed dams, they were crossfostered onto *ad-libitum* fed mothers. At weaning (age 21 days) pups were fed one of three diet regimes (normal, hypercaloric and hypocaloric (70% of normal)) *ad libitum* for the reminder of study. Around day 90 the systolic blood pressure was taken followed by the administration of growth hormone treatment for 21 days. It does not appear that this is an art accepted model to study the hypertension caused primarily by intrauterine under nutrition or growth retardation or an adverse postnatal environment because there is no evidence from prior art to indicate that this is an acceptable model. It is not predictable how the observations with Wistar rats would apply to other inbred rats, to

out bred rats, or to other species of animals, including humans. Nor is it clear to what real world conditions the experimental conditions relate.

The specification does not teach how one of ordinary skill in the art would recognize intrauterine under-nutrition in an adult suffering from hypertension. Specifically, what are the parameters one would use in the determination of intrauterine under-nutrition of a subject? Height and weight are rather variable in an out bred population, thus it is unclear what parameters can be used in the determination of under-nutrition of a subject for potential growth hormone treatment. In addition, there are babies who are born with low birth weight and shorter than average height who later on maintain the expected weight and height profiles. The amount of direction provided by the Applicant is inadequate to determine the nutrition status of the subject and the risk for potential hypertension. It is also unclear how growth retardation is measured: At what growth retardation levels will one choose to treat mammals/patients? Moreover, how does one determine whether growth retardation has occurred in a subject? The lack of adequate direction provided by the inventor and lack of working examples make this a non-enabling disclosure. Applicant indicates that consuming hypercaloric or hypocaloric diet constitutes an adverse postnatal environment (see page 5, lines 30-33). However, it is unclear how hypercaloric or hypocaloric a diet needs to be before one sees adverse postnatal environmental effects. Furthermore, it is not clear if any other conditions or events will affect the postnatal environment and thus cause hypertension to the subject. The disclosure does teach the symptoms of adverse postnatal

environment. Therefore, in the absence of adequate disclosure it would require undue experimentation to use the invention to treat hypertension.

Hypertension (in adult humans) is a multifactorial disease with diet, genetic history, smoking and other factors contributing to the disease state. Given the breadth of the claims, the teachings described in the specification are insufficient to enable one skilled in the art to practice the claimed invention without an undue amount of experimentation because these laboratory studies observed in rats are not predictive of success in clinical settings. The observations described in pages 8-10 will only serve as the basis for further experimentation. Since the therapeutic effect of growth hormone therapy is species and model-dependent, there is no predictability that the disclosed rat studies demonstrating hypertension induced by diet alone would serve as a valid model to study hypertension in mammals caused by intrauterine under nutrition or growth retardation or an adverse postnatal environment. Furthermore, there is no indication that the studies accurately predict the effect of growth hormone in the dynamic environment of an adult human. It is generally accepted that hypertension in humans is a multifactorial disease with the involvement of diet, genetic make up, smoking and other factors.

Applicant has not disclosed how to use the claimed invention to treat the hypertension of mammals other than a single strain of rat. There is insufficient disclosure of the invention with respect to the operability of the claimed invention. In addition, there is no guidance provided in choosing the therapeutically effective amount

for administering to the subjects. Applicant recites a broad, arbitrary, range with no evidence of the amount necessary to achieve the desired clinical effect.

Pharmaceutical therapies are unpredictable for the following reasons; (1) the proteins may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half life protein; (2) the protein may otherwise not reach the target area because, for example, the protein may not be able to cross the mucosa; (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo use*, i.e. may produce adverse side effects prohibitive to the use of such treatment.

Since applicant has not provided any working examples of the efficacy of treating already established hypertensive subjects except the rats in which hypertension was induced by the diet provided in the controlled experimental setting, it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

Given the breadth of claims 1 and 2, in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for treating hypertension in all mammals. In addition, due to the lack of established protocols for effective growth hormone therapies for hypertension caused primarily by intrauterine under nutrition or growth retardation or an adverse postnatal

environment, undue experimentation would be required to practice the claimed invention and would have little expectation of success.

Claim Rejections - 35 USC §102

6a.The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6b. Claims 1, 2, 4-6, 8, 11 and 12 rejected under 35 U.S.C. 102(b) as anticipated by Johannsson et al. (1997).

The instant invention is directed to a method of treating hypertension in a mammal, which has experienced intrauterine under nutrition or growth retardation or an adverse postnatal environment by administering growth hormone.

Johannsson et al. (1997). describe the administration of recombinant human growth hormone to treat abdominally obese men and observe this reduces diastolic blood pressure (see abstract). The reference is silent on the condition of these individuals intrauterine or postnatal status. However, the preamble of the instant claims which recite intrauterine under nutrition or growth retardation or an adverse postnatal environment has no patentable weight because the specification has not taught how such a condition is determined and therefore breaths no life and meaning into the term. Thus, the reference teaches the limitation of treating hypertension in an adult mammal (human) by administering growth hormone to lower diastolic blood pressure and meets

the limitations of the method steps of the claims. Therefore, the instant invention is anticipated by Johannsson et al. (1997).

7. Claims 1-12 and 20-28 are not allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

JS
September 25, 2003